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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/502,224	05/17/2005	Mahendra S. Rao	UT-0048	1620

26259 7590 11/01/2007

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1633	

NOTIFICATION DATE	DELIVERY MODE
11/01/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

poreilly@licataandtyrrell.com

Office Action Summary	Application No.	Applicant(s)	
	10/502,224	RAO ET AL.	
	Examiner	Art Unit	
	Fereydoun G. Sajjadi	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 August 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) *5-10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/7/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Status

Applicants' response of August 13, 2007, to the non-final action dated March 12, 2007 has been entered. Claims 1-10 are pending in the application. No claims have been amended, cancelled, or newly added. Claims 5-10 remain withdrawn from consideration, with traverse. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01.

Claims 1-4 are currently under examination.

Response to Claim Rejections - 35 USC § 112 - Lack of Enablement

Claims 1-4 stand rejected under 35 U.S.C. 112, first paragraph as failing to comply with the enablement requirement. The rejection set forth on pp. 3-8 of the previous office action dated March 12, 2007 is maintained for reasons of record.

Applicants traverse the rejection, arguing: "Examples 1 through 5 of the instant specification were included to describe culture conditions under which a multi-differentiating progenitor cell type (not the instant claimed astrocyte restricted precursor cells) differentiates into multiple cells types including astrocytes, oligodendrocytes and neuronal cells. As taught at page 8 of the instant specification, it is under conditions in which other populations differentiate into neurons or oligodendrocytes (such as exemplified in Examples 1-5) that the instant claimed population of cells does not express A2B5 and differs from stem and progenitor populations in its expression of CD44 and its ability to differentiate into astrocytes. These Examples were not provided as enablement for the instant claimed cells and the Examiner's focus on only the Examples section of the application to suggest that the instant specification lacks enablement is incorrect." Applicants additionally state that pp. 8-9 of the specification describe various methods for isolating the claimed astrocyte restricted precursor cells and pp. 11-15 describe various methods for using the cells, thus meeting the enablement requirement of 35 U.S.C. 112, first paragraph. Applicants' arguments have been fully considered, but are not found persuasive.

The previous office action outlined the basis for the rejection of the claims based on the lack of an enabling disclosure for a pure homogenous population of mammalian astrocyte

restricted precursor cells that are CD44 positive, (A2B5 negative), and can differentiated into astrocytes, but not oligodendrocytes, or a method of isolating the same from embryonic or fetal tissue, ES cell cultures, or glial restricted precursor cells as claimed. The claimed cells are not in accord with the observations in the working examples and the teachings of the prior art. Examples 1-5 of the instant specification describe the culture of human neural progenitor cells from fetal tissue, obtained from a commercial source. To isolated human neuroepithelial precursor cells (hNEPs), the cells were cultured for 5 days and subjected to immunopanning and FACS sorting to remover NCAM+, NG2+ and A2B5+ cells (Example 2). The cells negative for said markers were then propagated and plated on fibronectin/laminin coated coverslips in various conditions to promote differentiation. For astrocytic differentiation, cells were cultured for 5 days in the presence of 10%FCS, and astrocytes were identified using antibodies to CD44, GFAP and S-100. For oligodendrocyte differentiation, cells were plated in a bFGF containing medium for two days and then switched to a medium containing PDGF and T3 for 7 days. Therefore, at least for the human neuroepithelial progenitor cells, it is clear that following marker sorting, the same cell population may be differentiated to give rise to astrocytes and oligodendrocytes, depending on alterations in culture conditions. Hence, the human neuroepithelial progenitor cells are not astrocyte restricted, as they may differentiate into additional cells types. Moreover, the progenitor cells are capable of differentiation into oligodendrocytes, as taught by the specification, contrary to the language of the instant claims. In addition, the prior art of Raff et al. and Carpenter showed that neuroprogenitor cells differentiate into astrocytes or other neural cells depending on culture conditions.

Furthermore, the previous office action addressed the limitation of CD44 marker present on the instantly claimed precursor cells, as Lodie et al. (Tissue Eng. 8:739-751; 2002) teach that in human bone marrow derived stem cells, CD44 expression is variable, and apparently dependent on serum concentration (Abstract). The authors further demonstrated that CD44 expression did not have an impact on the ability of the cells to ultimately differentiate toward the neural lineage and appeared to be dependent on serum concentration as demonstrated by other researchers (pp. 749-750, bridging).

Regarding Applicants' argument that pp. 8-9 of the specification describe various methods for isolating the claimed astrocyte restricted precursor cells, it is noted that this section

of the specification is directed to isolation of CD44 positive cells from mammalian neural tubes at a stage after astrocyte development, and further, the variability in CD44 expression as dependent on serum concentration has been addressed on the record. Pp. 8-9 of the instant specification do not describe the isolation of a pure homogenous population of astrocyte restricted precursor cells that are at once A2B5 negative and CD44 positive, and possession of such a population at the time of invention by Applicants cannot be demonstrated.

Applicants have essentially argued that a person of skill in the art should not regard the working Examples as enabling for the instantly claimed invention, and thus particularly ignore Example 2, titled: "Isolation of Human Neuroepithelial Precursor Cells", that includes the isolation of A2B5 negative cells. However, a person of skill in the art having considered the teachings of the entire specification, would not find sufficient guidance for making the instantly claimed pure homogenous population of precursor cells that are at once A2B5 negative and CD44 positive, and restricted to only the astrocyte lineage, thus lacking the ability to generate oligodendrocytes. A person of ordinary skill having considered the teachings of the instant specification and the prior art would merely conclude that neuroepithelial precursor cells can differentiate into astrocytes, oligodendrocytes or other neural cells depending on culture conditions, and that any intermediate cell population of the final product (astrocytes) was not purified as a pure homogenous population of astrocyte restricted cells at the time of the instant invention by Applicants.

As the initial neuroprogenitor cells and their differentiation to the end product (astrocytes) were known and described in the prior art, any potential intermediates in the differentiation process must necessarily also be present. However, as indicated in MPEP 2112, The claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). >In In re Crish, 393 F.3d 1253, 1258, 73 USPQ2d 1364, 1368 (Fed. Cir. 2004).

Applicants further state that to address the issue regarding the CD44 positive cells of the instant invention being astrocyte restricted precursor cells, a post-filing publication by Liu et al. (Developmental Biology 2004 276:31-46; not previously of record) is submitted, which confirms that CD44 identifies an astrocyte restricted precursor cell that is committed to generating

astrocytes (see Abstract of Liu et al.). Such is not found persuasive, because MPEP 2164.05(a) states: "Specification Must Be Enabling as of the Filing Date". The state of the prior art provides evidence for the degree of predictability in the art and is related to the amount of direction or guidance needed in the specification as filed to meet the enablement requirement. The state of the prior art is also related to the need for working examples in the specification. The state of the art existing at the filing date of the application is used to determine whether a particular disclosure is enabling as of the filing date. > *Chiron Corp. v. Genentech Inc.*, 363 F.3d 1247, 1254, 70 USPQ2d 1321, 1325-26 (Fed. Cir. 2004) ("a patent document cannot enable technology that arises after the date of application").< Publications dated after the filing date providing information publicly first disclosed after the filing date generally cannot be used to show what was known at the time of filing. *In re Gunn*, 537 F.2d 1123, 1128, 190 USPQ 402,405-06 (CCPA 1976); *In re Budnick*, 537 F.2d 535, 538, 190 USPQ 422, 424 (CCPA 1976).

It is additionally noted that the post-filing art of Liu et al. describes using a CD44 misexpression transgenic mouse model and the misexpression of CD44 in culture to inhibit oligodendrocytes and arrest cells at the precursor state, thus providing evidence for the existence of $CD44^+$ astrocyte-restricted precursor cells in the developing nervous system (Abstract). Thus, Liu et al. did not demonstrate a pure homogenous population of astrocyte-restricted precursor cells in the absence of CD44 misexpression.

Therefore, the rejection of claims 1-4 is maintained for reasons of record and the preceding discussion.

Response to Claim Rejections - 35 USC § 102

Claims 1-4 stand rejected under 35 U.S.C. 102(e) as being anticipated by Carpenter (U.S. Patent No.: 6,833,269; filed May 31, 2001). The rejection set forth on pp. 8-10 of the previous office action dated March 12, 2007 is maintained for reasons of record.

The previous office action stated that claim language of "astrocyte restricted" is interpreted to be non-limiting because the ability of the cells to differentiate into astrocytes, but

not oligodendrocytes is a consequence of culturing conditions, as taught by the instant specification (Example 3, p. 17).

Applicants disagree with the rejection, arguing that "astrocyte restricted" is a limiting characteristic of the claimed invention which is not simply a consequence of culturing conditions, and argue that the wording Examples 1-5 were included to provide culture conditions, and refer to p. 8 of the specification and the teachings of post-filing of Liu et al. as confirming the teachings of the instant claims. Applicants' arguments have been fully considered, but are not found persuasive.

Applicant's arguments based on the teachings of p. 8 of the specification and post-filing art have been addressed (*supra*). In response to Applicants' arguments that Caprenter does not teach astrocyte-restricted neuroprogenitor cells that fail to generate oligodendrocytes, it is maintained that such a limitation is not afforded patentable weight in view of the foregoing discussion. Carpenter teaches methods for producing neural progenitor cells by culturing, expanding and differentiating embryonic stem cells into a variety of different neural phenotypes in a cocktail of growth conditions (Abstract). The method of Carpenter provides for the differentiation of pluripotent ES cells into cells of the neuronal or glial lineage. Precursor cells for either lineage, provide a source for generating additional precursor cells, neurons, astrocytes or oligodendrocytes (column 3; first paragraph), as well as neurons that include glial cells, astrocytes, dopaminergic cells and motor neurons (Abstract, column 19 and claim 18).

Additionally, CD44 expression is variable, and apparently dependent on serum concentration and culture conditions. Further the expression of CD44 is an inherent feature of the mammalian ES cell derived precursor cells of Carpenter et al. and must necessarily be present based on the culture conditions.

Therefore, the rejection of claims 1-4 is maintained for reasons of record and the preceding discussion.

Conclusion

Claims 1-4 are not allowed.

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR§1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fereydoun G. Sajjadi whose telephone number is (571) 272-3311. The examiner can normally be reached on 7:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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